

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 15:47:22 ON 11 DEC 2005

L1 2932 S ACETAL (S) (DEGRAD? OR BIODEGRAD? OR CLEAV? OR HYDROLYZ?)
L2 305 S L1 (S) (POLYMER OR COPOLYMER OR CO-POLYMER)
L3 2 S L2 (P) (DNA OR RNA OR NUCLEIC OR PLASMID OR POLYNUCLEOTIDE)
L4 36526 S POLYCATION OR POLYLYSINE OR POLYETHYLENEIMINE OR PEI
L5 6302 S L4 (P) (POLYMER OR COPOLYMER OR CO-POLYMER)
L6 156 S L5 (P) (ACETAL OR IMINE OR HYDRAZONE)
L7 15 S L6 (P) (ESTER OR PHOSPHOESTER OR AMIDE OR ANHYDRIDE OR URETH
L8 7 S L7 (P) (DNA OR RNA OR NUCLEIC OR PLASMID OR POLYNUCLEOTIDE)
L9 4 DUP REM L8 (3 DUPLICATES REMOVED)
L10 2 DUP REM L3 (0 DUPLICATES REMOVED)

AU Jon Sangyong; Anderson Daniel G; Langer Robert
SO Biomacromolecules, (2003 Nov-Dec) 4 (6) 1759-62.
Journal code: 100892849. ISSN: 1525-7797.

TI Degradable poly(amino alcohol esters) as potential DNA vectors with low cytotoxicity.

AB The synthesis of a new degradable polymer system, poly(amino alcohol esters) and the resulting polymers' potential for use in gene transfection vectors are reported. The polymerization proceeded in a one step reaction from commercially available bis(secondary amines) monomers (N,N'-dimethyl-1,3-propanediamine and N,N'-dimethyl-1,6-hexanediamine, respectively) through nucleophilic addition to the diglycidyl ester of dicarboxylic acid (diglycidyl adipate). Poly(amino alcohol ester) 1 and 2 were synthesized with a yield of 89% and 91% with Mn = 24,800 and Mn = 36,400, respectively. Poly(amino alcohol ester) 1 degraded hydrolytically in phosphate buffer at pH 7.4 with a half-life of approximately 5 days. Both polymers readily self-assembled with plasmid DNA into nanometer-sized DNA/polymer complexes less than 180 nm diameter and are significantly less cytotoxic than the commonly used DNA delivery polymer, poly(ethylene imine) (PEI).

AU Shuai, Xintao; Merdan, Thomas; Unger, Florian; Wittmar, Matthias; Kissel, Thomas
SO Macromolecules (2003), 36(15), 5751-5759
CODEN: MAMOBX; ISSN: 0024-9297

TI Novel Biodegradable Ternary Copolymers hy-PEI-g-PCL-b-PEG: Synthesis, Characterization, and Potential as Efficient Nonviral Gene Delivery Vectors

AB Diblock copolymers (MPEG-b-PCLs) of poly(.epsilon.-caprolactone) (PCL) and monomethoxyl poly(ethylene glycol) (MPEG) were synthesized by the conventional ring-opening polymn. of .epsilon.-caprolactone using MPEG as a macroinitiator. The monohydroxy-bearing diblock copolymers were reacted first with maleic anhydride and then with N-hydroxysuccinimide (NHS) to yield activated succinimidyl carbonate derivs. that are reactive with the primary amino group. Subsequently, a new class of biodegradable amphiphilic copolymer (hy-PEI-g-PCL-b-PEG) was prepd. by grafting the activated PCL-b-PEG onto the hyperbranched poly(ethylene imine) (hy-PEI). Thermal properties of bulk graft copolymers were investigated using differential scanning calorimetry and thermogravimetric anal. Depending on their compns., these polymers are completely sol. in water or form micelles of tens to hundreds of nanometers in size in the studied concn. range, as revealed by surface tension and dynamic light scattering measurements of copolymer solns. Complexation of plasmid DNA (pDNA) with various copolymers was investigated to achieve particles of ca. 200 nm diam. (N/P = 7). Copolymer compn. was found to affect significantly the gene transfection efficiency of polyplexes. In general, low graft d. and high mol. wt. of PEI blocks favor high gene transfection efficiency. All DNA/copolymer complexes (N/P = 7) showed a much lower .xi.-potential (i.e., neutral or neg.) than the DNA/PEI25 kDa complex (21 mV), indicating lower toxicity of copolymer-based complexes. Lower cytotoxicity of DNA/copolymer complexes was also demonstrated by the viability of cells in the transfection expts. These results indicate that these ternary copolymers are promising candidates for gene delivery, featuring

good biocompatibility, potential biodegradability, and relatively high gene transfection efficiency. Their neutral surface charge offers potential for i.v. administration.

- AU Seo, Dong Hoan; Kim, Seon Hwa; Khang, Gilson; Chi, Sang Cheol; Shin, Byung Cheol; Kim, Moon Suk
SO Polymer (Korea) (2005), 29(2), 135-139
CODEN: POLLDG; ISSN: 0379-153X
TI Preparation of PEG-folate-graft-polyethylenimine as a gene carrier
AB Poly(ethylene imine) (PEI) modified by methoxypoly(ethylene glycol) (mPEG) and folate as a gene carrier was synthesized to decrease cytotoxicity and to improve in vivo targeting. MPEG was modified by glutaric anhydride (GA) to endow carboxylic end group, followed by the activation reaction with EDC (N-ethyl-N'-(3-dimethylaminopropyl) carbodiimide) and NHS (N-hydroxysuccinimide). The activated carboxylic end group of mPEG was reacted with the amines of PEI to give mPEG graft PEI. The mPEG-folate-graft-PEI was synthesized by the reaction of mPEG-PEI with folate pre-activated by EDC/NHS. The obtained copolymers were characterized by ¹H-NMR and FT-IR. Gel retardation assay and fluorescence measurement indicated that DNA formed the complexes with the synthesized copolymers above N/P charge ratio 2. The size of complexes was ranging from 100 nm to 300 nm. We confirmed that the synthesized copolymer have the possibility as a DNA carrier.
- IN Kataoka, Kazunori; Nagasaki, Yukio; Shibata, Naoya; Hoshino, Nobuhiro
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
TI Functionalization of polylactide (PLA) surface using end-functionalized block copolymer of .alpha.-acetal-poly(ethylene glycol) (PEG)/PLA
AB A method of binding a substance to the free ends of water-sol. polymer chains which are bonded at the other ends to a substrate surface so as to form a brush-like structure and have, at the free ends, reactive functional groups capable of reacting with the substance to be incorporated, by reacting the substance to be incorporated with the reactive functional groups in the presence of a water-sol. polymer which has the ability to accelerate the binding, is disclosed. Proteins, DNA, or cells may be incorporated by reacting with a terminal aldehyde group of PEG immobilized on latex particle or macromol. micelle. This paper deals with novel approaches established for the construction of a functionalized poly(ethylene glycol) (PEG) layer, PEG-brushed layer possessing a reactive group at the free end to tethered PEG chain, on substrates. An AB-type block copolymer composed of .alpha.-acetal-poly(ethylene glycol) (PEG) as the hydrophilic segment and polylactide (PLA) as the hydrophobic segment was synthesized, and utilized to construct the functionalized PEG layer on the biodegradable polylactide surface by simple coating. In this way, a PEG-brushed layer with a terminal aldehyde group was readily prepd. which may have both non-fouling and ligand-binding properties. Based on the characterization of these PEGylated surfaces from a physicochem. (contact angle, potential, ESR) as well as biol. (protein adsorption) point of view, the authors' strategy to construct a functionalized PEG layer was confirmed. Active functional groups were present at the tethered PEG-chain end, these materials will have a high utility in the biomedical field. Attachment of bovine serum albumin and anti C-reactive protein (CRP) rabbit antibody F(ab') fraction, in the presence of PEG6000, is described.
- AU Murthy, Niren; Stayton, Patrick S.; Hoffman, Allan S.
SO Polymer Preprints (American Chemical Society, Division of Polymer Chemistry) (2000), 41(1), 1010-1011
CODEN: ACPPAY; ISSN: 0032-3934
TI pH sensitive membrane disruptive PEGylated polycations
AB A new method for the synthesis of novel PEGylated pH sensitive membrane-disruptive polycations as potential oligonucleotide delivery vehicles has been presented. The strategy is based on grafting PEG onto a hydrophobic-polycationic backbone through an acid degradable acetal linkage. The acetal linkage used for the PEGylation of Copolymer I had a half life of 15 min at pH 5.4, but at pH 7.4 less than 10% of the acetals were hydrolyzed after 80 min. Copolymer I has a hydrolysis rate suitable for drug delivery purposes. The hydrolysis of the PEG grafts and activation of its membrane

disruptive activity occur in less than 20 min at pH 5.0. Copolymer I was membrane disruptive at pH 5.0 but not at pH 7.4. The above copolymers should therefore have applications for the delivery of neg. charged polyanions such as DNA or ODNs to cells.

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1917	acetal with (\$degrad\$ OR \$cleav\$)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/11 13:47
L2	516	l1 with (polymer OR copolymer OR co-polymer)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/11 13:57
L3	6	l2 same (dna OR rna OR nucleic OR plasmid OR polynucleotide)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/11 13:49
L4	550241	polycation OR polylysine OR poly(ethyleneimine) OR PEI	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/11 13:56
L5	173817	l4 same (polymer OR copolymer OR co-polymer)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/11 13:57
L6	8492	l5 same (acetal OR imine OR hydrazone)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/11 13:58
L7	4135	l6 same (ester OR phosphester OR amide OR anhydride OR urethane)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/11 13:58
L8	30	l7 same (dna OR rna OR nucleic OR plasmid OR polynucleotide)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/11 13:58
L10	2	"20050054604"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/11 15:17
S1	19324	polycation OR polylysine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/11 13:56
S2	5891	S1 same polymer	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/08 16:06
S3	276	S2 same (acetal OR imine OR hydrazone)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/08 16:07
S4	54	S3 same (ester OR phosphester OR amide OR anhydride OR urethane)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/08 16:33

S5	19	S4 and (DNA or RNA)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/08 16:09
S6	1	("6290947").PN.	USPAT	OR	OFF	2005/12/10 20:59
S7	216	sheng near2 li.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/10 21:00
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S9	24	sang near2 van.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/10 21:29
S10	1	("6337227").PN.	USPAT	OR	OFF	2005/12/10 21:20
S11	2	"20040198678"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/12/11 15:17